Heart Failure Update: Diastolic Dysfunction

William T. Abraham, MD, FACP, FACC, FAHA
Professor of Medicine, Physiology, and Cell Biology
Chief, Division of Cardiovascular Medicine
Deputy Director, Davis Heart & Lung Research Institute
The Ohio State University
Columbus, Ohio

Heart Failure Hospitalizations are Increasing

Epidemiology of Symptomatic Heart Failure in the United States

• ≈ 5 million Americans with heart failure
• 400,000 - 700,000 new cases diagnosed/year
• Most frequent cause of hospitalization in patients older than 65 years
• Primary reason for 12 to 15 million office visits and 6.5 million hospital days each year
• Causes or contributes to 250,000 deaths/year
• 1-Year mortality rate is about 10-15%
• 5-Year mortality rate approaches 50%

Decompensated Heart Failure: The Major Contributor to Cost of Care

Episodes of decompensation ($36 B)
- Hospital care
- MD visits
- ED visits
- Dx testing

Maintenance ($18 B)
- Medications
- Routine MD visits
- Nonmedical care

Surgical procedures to treat HF ($4.2 B)
- Heart transplantation
- Mechanical devices

Total HF cost: $56 billion

O’Connell JB. Clin Cardiol 2000;23:III-6

SOURCE: Hospital discharges include patients both living and dead.
AHA Heart and Stroke Statistical Update 2001
Outcomes in Patients Hospitalized With Heart Failure

**Hospital Readmissions**

- 0 days: 20%
- 6 months: 50%

**Mortality**

- 30 days: 12%
- 12 months: 33%
- 5 years: 50%

N = 38,702
Aghababian RV. Rev Cardiovasc Med 2002; 3:S3

The ADHERE Registry

- **ADHERE** (Acute Decompensated HEart Failure National REgistry) was a prospective, observational database of patients hospitalized with acutely decompensated heart failure
- Over 275 US hospitals participated in this project, including community, tertiary, and academic medical centers
- More than 200,000 patients were enrolled in ADHERE

Acute Exacerbations Contribute to the Progression of the Disease

With each event, hemodynamic alterations/myocardial injury contribute to progressive ventricular dysfunction and dilation

Jain P et al., Am Heart J. 2003;145:S3-S17

Characteristics of Heart Failure Patients Enrolled in the ADHERE Registry

- Average age: 72.5 years
- Women: 52%
- Ischemic etiology (CAD): 60%
- Renal insufficiency: 30%
- Preserved LV systolic function: ≈50%
- Atrial fibrillation: 31%
- Diabetes: 44%
Heart Failure with a Normal Ejection Fraction

- High proportion (50%) of patients with congestive heart failure have normal LV systolic function
- Variably called diastolic heart failure (DHF), heart failure with preserved ejection fraction (HFPEF), and heart failure with normal ejection fraction (HFNEF)

Diastolic Heart Failure: Diagnosis

1. Signs and symptoms of CHF
2. Normal LV ejection fraction
3. Measurement of diastolic function is confirmatory but not mandatory

Heart Failure with a Normal Ejection Fraction

- Hospital admission rates for patients with diastolic heart failure are similar to systolic heart failure
- There is no gold standard for diagnosis of DHF and no standardized treatment

Causes of Diastolic Heart Failure

- Pericardial Disease
  - Constriction
  - Tamponade
- Restrictive Heart Disease
  - Infiltrative
  - Idiopathic
Causes of Diastolic Heart Failure

- Ventricular Hypertrophy
  - Primary (genetic)
  - Secondary (acquired)
- Ventricular Aneurysm

Risk Factors for Diastolic Heart Failure

- Aging
- Hypertension
- Diabetes
- Coronary Artery Disease
- Obesity
- Obstructive Sleep Apnea
- Others

Is HFNEF One Pathophysiologic Entity?

- Idiopathic Hypertrophic Cardiomyopathy
- Infiltrative Diseases
  - Amyloid
  - Sarcoid
  - Hemochromatosis
- Hypertensive Hyper trophy
  - Hypertensive Heart Disease (??)

Heart Failure with Normal Ejection Fraction: Differential Diagnosis of Underlying Mechanisms and Contributing Factors*

- Diastolic heart failure (DHF)
  - Restrictive cardiomyopathy
  - Infiltrative cardiomyopathy
  - Amyloid
  - Hemochromatosis
  - Hypertrophic cardiomyopathy
  - Hypertrophic Heart Disease (??)

- Hypertensive heart disease not due to diastolic dysfunction
  - Volume Overload State with causal or contributing factors:
    - Chronic Renal Dysfunction
    - Salt/Water Handling Abnormality
    - Anemia
    - Ventricular Vascular Coupling Abnormality (??)
    - Excessive Venoconstriction

- Right heart failure
  - Pericardial disease
  - Intracardiac mass
  - Valvular heart disease

**DHF: LV Response to Heart Rate**

- Relaxation Rate
- Diastolic Pressure

**Left Atrial Pressure Changes with Exercise**

**DHF: LV Response to Volume Loading**

- DHF: \( P = 1.5 \times e^{(0.034V)} \)
- Normal: \( P = 2.3 \times e^{(0.010V)} \)

Zile M et al., NEJM 2004
### ACC/AHA 2005 Guideline Update for the Management of Patients With Chronic Heart Failure in the Adult

**Writing Committee Members**

<table>
<thead>
<tr>
<th>William T. Abraham, MD, FACC, FAHA</th>
<th>Donna M. Mancini, MD</th>
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<tr>
<td>Marshall H. Chin, MD, MPH, FACP</td>
<td>Keith Michl, MD, FACP</td>
</tr>
<tr>
<td>Arthur M. Feldman, MD, PhD, FACC</td>
<td>John A. Oates, MD, FAHA</td>
</tr>
<tr>
<td>Gary S. Francis, MD, FACC, FAHA</td>
<td>Peter S. Rahko, MD, FACC, FAHA</td>
</tr>
<tr>
<td>Theodore G. Ganiats, MD</td>
<td>Marc A. Silver, MD, FACC, FAHA</td>
</tr>
<tr>
<td>Mariell Jessup, MD, FACC, FAHA</td>
<td>Lynne Warner Stevenson, MD, FACC</td>
</tr>
<tr>
<td>Marvin A. Konstam, MD, FACC</td>
<td>Clyde W. Yancy, MD, FACC, FAHA</td>
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### Stage C Therapy

**Normal LVEF with Symptoms**

**Recommended Therapies for Routine Use:**

- Treating known risk factors (e.g., hypertension) with therapy consistent with contemporary guidelines
- Ventricular rate control for all patients with AF
- Drugs for all patients
  - Diuretics

### AHA/ACC Applying Classification of Recommendations and Level of Evidence

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
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<tbody>
<tr>
<td>Benefit &gt;&gt;&gt; Risk</td>
<td>Benefit &gt;&gt; Risk with focused objectives needed</td>
<td>Benefit &gt;&gt; Risk Additional studies with broad objectives needed; Additional registry data would be helpful</td>
<td>Risk z Benefit No additional studies needed</td>
</tr>
<tr>
<td>Procedure or treatment SHOULD be performed or administered</td>
<td>IT IS REASONABLE to perform procedure or administer treatment</td>
<td>Procedure or treatment MAY BE CONSIDERED</td>
<td>Procedure or treatment should NOT be performed or administered SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL</td>
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**Level of Evidence**

- A: Multiple randomized controlled trials
- B: Single trial, non-randomized studies
- C: Expert opinion

### Stage C Therapy

**Normal LVEF with Symptoms**

- Drugs for appropriate patients
  - ACEI
  - ARBs
  - Beta-Blockers
  - Digitalis
- Coronary revascularization in selected patients
- Restoration/maintenance of sinus rhythm in appropriate patients
Differential Diagnosis in Patient with HF and Normal LVEF with Symptoms

- Incorrect diagnosis of HF
- Inaccurate measurement of LVEF
- Primary valvular disease
- Restrictive (infiltrative) cardiomyopathies
- Amyloidosis, sarcoidosis, hemochromatosis
- Pericardial constriction
- Episodic or reversible LV systolic dysfunction
- Severe hypertension, myocardial ischemia
- HF associated with high metabolic demand (high-output states)
- Anemia, thyrotoxicosis, arteriovenous fistulae
- Chronic pulmonary disease with right HF
- Pulmonary hypertension associated with pulmonary vascular disorders
- Atrial myxoma
- Diastolic dysfunction of uncertain origin
- Obesity

Physicians should control systolic and diastolic hypertension in patients with HF and normal LVEF, in accordance with published guidelines.

Stage C Therapy Normal LVEF with Symptoms

Ventricular Rate Control

Physicians should control ventricular rate in patients with HF and normal LVEF and atrial fibrillation.

Diuretics

Physicians should use diuretics to control pulmonary congestion and peripheral edema in patients with HF and normal LVEF.
**Stage C Therapy**

**Normal LVEF with Symptoms**

### Coronary Revascularization

Coronary revascularization is reasonable in patients with HF and normal LVEF and coronary artery disease in whom symptomatic or demonstrable myocardial ischemia is judged to be having an adverse effect on cardiac function.

### Angiotensin Enzyme Converting Inhibitors (ACEIs)

The use of beta-adrenergic blocking agents, ACEIs, ARBs, or calcium antagonists in patients with HF and normal LVEF and controlled hypertension might be effective to minimize symptoms of HF.

### Restoration/Maintenance of Sinus Rhythm

Restoration and maintenance of sinus rhythm in patients with atrial fibrillation and HF and normal LVEF might be useful to improve symptoms.

### Angiotensin Receptor Blockers (ARBs)

The use of beta-adrenergic blocking agents, ACEIs, ARBs, or calcium antagonists in patients with HF and normal LVEF and controlled hypertension might be effective to minimize symptoms of HF.
### Stage C Therapy

**Normal LVEF with Symptoms**

#### Beta-Blockers

The use of beta-adrenergic blocking agents, ACEIs, ARBs, or calcium antagonists in patients with HF and normal LVEF and controlled hypertension might be effective to minimize symptoms of HF.

<table>
<thead>
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<th>Strength</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>III</td>
<td>IIa</td>
</tr>
<tr>
<td>IIa</td>
<td>IIb</td>
</tr>
<tr>
<td>IIb</td>
<td>III</td>
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#### Digitalis

The usefulness of digitalis to minimize symptoms of HF in patients with HF and normal LVEF is not well established.

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<td>IIb</td>
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<td>IIb</td>
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### Novel Approach to Managing Diastolic Heart Failure

### Implantable Hemodynamic Monitors

- LV Pressure Sensor
- PA Pressure Sensors
- RV Pressure Sensors
- LA Pressure Sensors
RV Monitoring System and Information Flow

- RV Systolic Pressure
- RV Diastolic Pressure
- Estimated PA Diastolic Pressure
- Other Parameters

COMPASS- HF Trial: Primary Endpoint

<table>
<thead>
<tr>
<th>CHRONICLE (n=134)</th>
<th>CONTROL (n=140)</th>
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<tbody>
<tr>
<td>Pts with Events</td>
<td>44</td>
</tr>
<tr>
<td>Total HF-Related Events</td>
<td>84</td>
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<tr>
<td>Hospitalizations</td>
<td>72</td>
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<tr>
<td>Emergency Dept Visits</td>
<td>10</td>
</tr>
<tr>
<td>Urgent Clinic Visits</td>
<td>2</td>
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<tr>
<td>Event Rate / 8 months</td>
<td>0.87</td>
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<tr>
<td>% Reduction in Event Rate</td>
<td>21%</td>
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p=0.33

RV Pressure Monitor: Correlation to Swan Ganz

- Systolic
- Diastolic
- ePAD

PA Pressure Sensor

- Un-powered, implantable wireless pressure sensor
- Implanted in the distal pulmonary artery
- Pressure measurements performed at home or in the physicians office using simple RF based electronics
- Pressure data automatically forwarded to physician, can be viewed on custom website portal

PA Sensor vs Swan Ganz

Regression Plot of Sensor vs. SG Mean Pressure Measurements for 16 Patients

\[ R^2 = 0.961 \]

SG reading (mm Hg)

Sensor reading (mm Hg)

Implantable LA Pressure Monitor

Implantable Sensor Lead (ISL)

Proximal Anchor

Sensor Diaphragm ~ 3 mm

Measures

- LAP
- IEGM
- Core Temp

LAP Accuracy VS. PCWP

LAP = 0.94xPCWP + 2.0

\[ R^2 = 0.95 \]

n=429

PCWP (mmHg)

LAP (mmHg)

NTG

Rest

Provocation

Valsalva

Mean of LAP and PCWP (mmHg)

LAP-PCWP (mmHg)

\[ \text{mean} = 0.5 \text{ mmHg} \]

\[ \pm 2 \text{ SD} = 9.0 \text{ mmHg} \]

n=429

Patient Management Using the LAP Monitoring System

Patient obtains LAP readings twice a day with PAM at rest & supine prior to meds

LAP data uploaded to Clinician’s PC Software

Objective = Control LAP Excursions

Patient uses DynamicRx to self-titrate HF meds

Clinician formulates DynamicRx based on LAP data
**IHM Patient Advisory Module**

Modified PDA
- Powers through clothing
- Atmospheric reference
- Stores telemetry
- Alerts patient to monitor
- 'DynamicRX' instructs
  - Meds
  - Activity
  - Clinician contact
  based on LAP values and physician's prescription

**Summary**

- Diastolic heart failure is common, comprising 50% of heart failure in general
- Control of fluid volume and heart rate and promotion of regression of LV hypertrophy are the main goals of empirical therapy
- Newer (investigational) technologies promise to improve the treatment of this disorder

**Trend plot on Dynamic Rx**

<table>
<thead>
<tr>
<th>Date</th>
<th>LAP (mmHg)</th>
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<tbody>
<tr>
<td>Jul-05</td>
<td></td>
</tr>
<tr>
<td>Aug-05</td>
<td></td>
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<tr>
<td>Sep-05</td>
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<tr>
<td>Mar-06</td>
<td></td>
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<tr>
<td>Apr-06</td>
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- Observation AM
- Observation PM
- Titration AM
- Titration PM
- Dynamic AM
- Dynamic PM